RESPONSE TO OFFICE ACTION

A. Status of the Claims

Claims 1, 5-8, 10-14, 17-22, 26-33, 35-41, 43-45, 49-52, and 54 are pending. Claims 19 and 49 have been amended. Support for the amendments is found in the claims as filed and, for example, at page 7, line 12 of the specification. No new matter has been added. Thus, claims 1, 5-8, 10-14, 17-22, 26-33, 35-41, 43-45, 49-52, and 54 are presented herein for reconsideration.

B. Specification Objections

The Action has objected to the Specification for use of the term "Parafilm M". In response it is noted that the Specification has been amended as suggested, by capitalizing the term to clarify its status as a trademark. Withdrawal of the objection is respectfully requested.

C. Claims rejection under 35 U.S.C. § 112, second paragraph- indefiniteness.

The Action asserts that claim 19 and 49 are indefinite in that claim 19 as previously amended depends on a cancelled claim, while claim 49 contains a reference to the trademark/trade name PARAFILM M. In response, Applicants note that claim 19 has been amended to depend on claim 14. Additionally, claim 49 is amended to clarify the sealing material. Applicants submit that the rejections are moot, and respectfully request that they be withdrawn.

D. Claims rejection under 35 § 102(b)

Claims 1, 5-6, 8, and 10-12 are rejected under 35 U.S.C. § 102(b) as being anticipated by Smith *et al.* (*In Vitro* 13:329-334, 1977), in that Smith *et al.* are alleged to disclose a method of culturing cotton callus under conditions including in the dark and in the presence of isoascorbic acid. Applicants respectfully traverse as follows:

As an initial matter, Applicants note that the Smith *et al.* reference describes culture, and more specifically, callus initiation, of plant cells from *Gossypium arboreum*, a diploid wild relative, and not of regenerable cells of the widely cultivated cotton crop species (*Gossypium hirsutum*, a tetraploid) exemplified by variety Coker 312 as described in the Specification, for instance, at page 24, line 13. Further, the reference explicitly notes at page 330, left column, first full paragraph, and at page 333, right column top paragraph, that conditions for establishing and maintaining callus cultures of *G. arboreum* being reported by the paper vary from cotton media described by earlier workers, such as for *G. hirsutum,* indicating that cell culture requirement for *G. arboreum* are distinct from those with other *Gossypium* species.

Further, the cited reference is not concerned with culturing of regenerable embryogenic or non-embryogenic cotton cells. No where in the reference is there described any regeneration of plants from their *G. arboreum* callus cell cultures, or an ability of their callus cell cultures to regenerate. Callus initiation and embryogenesis/regeneration are known to be distinct physiological states for cotton cell cultures, and represent separate barriers in terms of the progress toward achieving transgenic cotton plants. Thus, the reference would clearly not be considered by one of skill in the art of plant cell culture to necessarily teach any specific conditions for regenerable cotton crop cell culture. Applicants submit that the reference of Smith *et al.* does not recite all of the limitations of the present claims, in particular the use of regenerable cotton tissue, and thus does not anticipate the present claims. Withdrawal of the rejection made in view of Smith *et al.* is thus respectfully requested.

Regarding the growth of cotton callus under the light conditions as described by Smith *et al.,* Applicants note that in every case reported in Smith Table 1, low light yielded much poorer growth than high light conditions, while data from cell growth in dark conditions is not even shown.

Further, the Smith reference states: "The best environmental conditions observed for callus proliferation from hypocotyl tissue were under high light as compared to total darkness…" (Smith, page 333, left column, 2nd full paragraph). This clearly teaches away from the data of the present application, to the extent that one of skill in the art would even apply Smith's teachings for *G. arboreum* callus initiation to any attempt to culture cells from another cotton crop species, or to regenerable cotton crop cell cultures. That is, if one followed the teachings of Smith in regards to light intensity, one would not be practicing the invention being claimed (*e.g.* claims 1, 5-6) and that are being rejected for this reason by the Action. Removal of the rejection in this regard is thus respectfully requested.

Regarding claims 8 and 10-12, and the growth of cotton callus in the presence of isoascorbic acid (also known as erythorbic acid), Applicants note first, that isoascorbic acid and ascorbic acid are distinct compounds (CAS Registry Numbers 89-65-6 and 50-81-7, respectively), and thus any routine analogy between the use of the isomers is not apt. For instance, the cited reference, in the sentence bridging pages 329-330, reports that the levels of ascorbic and isoascorbic acid that were utilized in a described reference (Davis *et al. In Vitro* 9:395-398, 1974) are quite different (5 mg/l and 100 mg/l, respectively), indicating again that they are not readily interchangeable.

One of skill in the art simply would not consider the two isomers to be interchangeable as plant cell culture ingredients, whether in *G. arboreum,* or in cotton crop cell cultures. Indeed, Smith *et al.* note at page 331, right column, 3rd paragraph, that incorporation of isoascorbic acid into growth media "…not only failed to enhance callus growth for *G. arboreum*, but in fact resulted in reduced callus proliferation at all concentrations". Further, at page 333, left column lines 14-16, the Smith reference explicitly states that "…contrary to this we find no requirement for a reducing agent [*e.g.* isoascorbic acid] for callus growth…." [emphasis added].

This can be compared, if at all, to the effect reported for the use of ascorbic acid in the present application, for instance at Table 4, page 27, where ascorbic acid increased total frequency of embryogenesis in cotton cell culture. If anything, the report of Smith *et al.* and its use of isoascorbic acid with *G. arboreum* cells would teach away from the methods described in the present application regarding use of ascorbic acid with Coker 312-derived cells. Thus, with respect to its teachings regarding the species of *Gossypium* being studied and their regenerability, as well as dark/light growth conditions and use of isoascorbic acid, the Smith reference simply does not anticipate the present application, and Applicants respectfully request that the claims rejection under 35 U.S.C. §102(b) in view of this reference be removed.

The Action also rejects claims 1 and 5 under 35 U.S.C. §102(b) as being anticipated by Hirimburegama *et al.* (*J. Nat. Sci. Council Sri Lanka* 22:305-315, 1994). The Hirimburegama reference is stated to disclose a method for culturing cotton tissue in complete darkness. Applicants respectfully traverse as follows:

The Hirimburegama reference does not describe regenerable cell cultures of cotton (*G. hirsutum*). Instead, the reference describes efforts to establish cotton callus cultures for the purpose of "possible plant regeneration" (Hirimburegama, page 305, 2nd paragraph, last sentence of Introduction; emphasis added). No where does this reference describe any of the established cell cultures as having led to the regeneration of a cotton plant (*i.e.* that they are regenerable callus cultures). Thus, this reference does not recite all of the limitations of the claims and does not anticipate the claimed invention. Removal of the rejection is thus respectfully requested.

E. Claims rejection under 35 U.S.C. § 103(a)

(1) The Action rejects claims 1, 5-6, 8, 10-12, 14, 17, 18, 39-41, 44, and 50-52 under 35 U.S.C. § 103(a) as being unpatentable over Smith *et al.*, in view of Adkins *et al.* (*J Exp Bot*

44:1829-1835, 1983). Applicants respectfully traverse, noting again that the Smith reference simply is not concerned with cell culture of the widely cultivated cotton crop species (*e.g.* of Coker 312), but rather with cells from another species, *G. arboreum*, and the reference explicitly distinguishes between the preferable culture conditions for the two different species.

Regarding the Adkins reference, Applicants note that it is concerned with rice cell culture. It would not have been obvious to one of skill in the art to routinely apply teachings related to rice (*i.e.* a monocot) cell culture to cotton (a distantly related dicot plant). As noted above, the conditions even for culture of cells from two species within the same genus, *G. arboreum* and *G. hirsutum*, could differ substantially. At most, a skilled worker might consider testing the effects on cotton cells of AVG and/or of an amino acid supplement such as casein hydrolysate, and/or of growth under darkness, but the cited reference would not lead one to expect beneficial results such as are described in the present application, or even motivate one to combine these various treatments for cotton cell culture.

The Adkins reference describes use of AVG for promoting callus growth, without showing how it would affect callus embryogenesis or regenerability. Further, Adkins Figure 2 allegedly shows an effect of AVG on callus growth. However, only one of the data points (1 mmol m^{-3} AVG) shows a positive effect on callus growth in the dark (and has the opposite effect on light grown material), while 5 mmol m^{-3} AVG decreases rice callus growth in the dark (but not the light). Given the clear sensitivity of rice callus to small changes in the level of AVG, and differential effects in dark and light, one of skill in the art would not routinely apply these teachings to any given rice culture attempt, let alone find it obvious to extrapolate to use of AVG in regenerable cotton cell culture.

The Action also alleges that Adkins describes an improvement in callus growth under dark conditions (Action page 5, referring to Adkins, p.1832 column 1 and page 1833, column 2). Applicants again note that this Adkins reference describes cell culture of the monocot plant rice, and not the dicot cotton. Further, at page 1831, right column, last paragraph, Adkins notes that

> "When pooling the data for all three cultivars, best conditions for growth were a combination of moderate temperatures (25°C) in the dark and the poorest conditions for growth were a combination of high temperature (35°C) in the light or in the dark [emphasis added],"

Thus any effect of culture in darkness is apparently tied to a temperature effect. Given that *G. arboreum cells* are apparently cultured under higher temperatures than rice cells, (*i.e.* the cited Smith reference describing *G. arboreum* cell culture states at page 333, left column, 2nd full paragraph that "..the best environmental conditions...were under high light as compared to total darkness and low light at 29±1°C"), and the differences in light responses for cell growth between *G. arboreum* and rice, a skilled worker simply would not reasonably consider the teachings of Adkins directly relevant to cotton cell culture, let alone combine the teachings with those of Smith, for the reasons described above. The Action further alleges that "selecting organic nitrogen source is an obvious decision choice", and that, "...the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art..." (Action, page 5, last paragraph). Applicants note that optimization of nitrogen source for growth could vary among different cell cultures derived from distantly related plants, and the Action provides no basis that rice cells and cotton cells respond similarly to the presence of a given amino acid supplement or organic nitrogen source.

Applicants respectfully submit that, for the various plant cell culture parameters noted in the preceding paragraphs, one of skill in the art would simply not find the cited references to be directly relevant and would have had no motivation to combine them. The references further do not lead one of skill in the art to a reasonable expectation of success, given the numerous cell culture

parameters involved. Finally, the references neither teach nor suggest all of the claims limitations, since, even if they were properly combined, none of these references describe regenerable cotton cell culture. The Action therefore has not established a factually supported *prima facie* case of obviousness in view of these references (MPEP 2142), and removal of the rejection is respectfully requested.

(2) The Action further rejects claims 7, 13, 20-22, 26-28, 31-33, 36-38, and 45 under 35 U.S.C. 103(a) as being unpatentable over Smith *et al.,* in view of Adkins *et al.* as applied to claims 1, 5-6, 8, 10-12, 14, 17-19, 39-41, 44, and 50-52, and further in view of Umbeck (U.S. Patent No. 5,004,863). Applicants respectfully traverse.

While the cited Umbeck patent relates to (*G. hirsutum*) cotton cell culture and transformation, information on cell culture relates primarily to selection conditions for identifying transformed cells, and culture in darkness is not described. In view of the numerous differences in culture conditions noted above for these various references being combined here, including cell genotype, light/dark growth response, temperature for growth, ability to undergo embryogenesis and regenerability, and nutritional and antioxidant requirements, to name a few of the possibly interacting parameters, one of skill in the art would not have been motivated to apply the teachings of Smith, in view of Adkins, to the method for culturing cotton tissue that is described by Umbeck, nor would one of skill in the art have had any reasonable expectation for success if they had done so.

Even if one had done so it would have been unclear as to which of the teachings, often contradictory between the references, would be followed in any case (*e.g.* growth in a 16 hour photoperiod as described by Umbeck; in darkness as allegedly described by Smith, although no data is provided and growth under such conditions is stated to be poor; or in light or darkness and at what

temperature as reported by Adkins in Figure 1, for rice). The Action simply provides no basis for how one of ordinary skill in the art would be expected to pick and choose among these numerous cell culture parameters to arrive at the invention being claimed, other than by hindsight. In contrast the present disclosure, for instance in the Examples 2-9 describes a set of conditions that ultimately result in improved frequencies of induction of embryogenesis and cotton embryo maturation and germination, resulting in plant formation (*e.g.* Table 10). Applicants thus respectfully submit that these references do not individually or in combination support a finding of obviousness, and request removal of this rejection.

(3) The Action rejects claims 29, 30, and 35 under 35 U.S.C. 103(a) as being unpatentable over Smith *et al.* in view of Adkins *et al.*, and further in view of Umbeck, and further in view of Dodds *et al.* (*Expt Pl Cell Culture* 2nd Ed. 1985). Applicants respectfully note that the Dodds reference is not related to cotton cell culture, and instead describes general methods that are not necessarily applicable to cotton cell culture, but would instead require specific additional experimentation to apply or to optimize with respect to cotton cell culture. Thus any methods described by Dodds are not necessarily or routinely applicable to cotton cell culture , and thus are not *prima facie* obvious to one of skill in the art.

For instance, while use of PARAFILM M or a given support medium such as filter paper might have been a formal possibility for a skilled cotton cell culture worker, its mention by Dodds in no way specifically motivates a skilled worker to investigate it use for cotton cell culture, nor does it reasonably show that any beneficial result would be obtained. Likewise regarding use of casein hydrolysate, Dodds states at page 39, last paragraph, that

> "...amino acids are not usually added to plant culture media...If a mixture of organic nitrogen is considered necessary, the medium can be enriched with ...casein hydrolysate...If the addition of the hydrolysate results in a beneficial effect,

additional experiments should be made...ultimately the specific organic nitrogen requirements can be identified."

This teaching of Dodds regarding casein hydrolysate appears to go against the alleged teachings of Adkins as described at page 5 of the Action. Again, no specific teachings relevant to cotton cell culture are given, and the skilled worker would have drawn no inference from Dodds regarding specific conditions for cotton cell growth. Nor would the worker have had any reasonable expectation of success in improving cotton cell culture growth based on these teachings. In sum, these references only demonstrate that the numerous often-interacting parameters for plant cell culture would lead one of skill in the art to be appropriately cautious in applying "general" teachings to culture of specific species, and especially to historically difficult-to-culture/regenerate species such as cotton. Thus Applicants respectfully request that the rejection be removed.

(4) The Action rejects claims 43 and 54 under 35 U.S.C. 103(a) as being unpatentable over Smith *et al.* in view of Adkins *et al.* as applied to claims 39 and 50, and further in view of Dodds. Applicants respectfully traverse.

Applicants note that none of the references cited for this rejection describe regenerable cotton cell culture, and thus the references as combined do not teach or suggest all of the claim limitations. As also noted above, a worker skilled in the art of cotton cell culture would further have had no motivation to combine them, nor any reasonable expectation of success in doing so. Applicants submit that the Action has therefore not provided a showing of *prima facie* obviousness in view of these references (MPEP 2142), and removal of the rejection is respectfully requested.

F. Conclusion

In view of the above, it is submitted that all of the rejections to the claims have been overcome, and the case is in condition for allowance.

The Examiner is invited to contact the undersigned at (512) 536-3085 with any questions, comments, or suggestions relating to the references patent application.

Respectfully submitted,

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